Response to Rejection under 35 U.S.C. §§102(b) and 102(e)

Claims 1-14 stand rejected under 35 U.S.C. §§102(b) and 102(e) as being anticipated by Ekins *et al.* (U.S.P.N. 5,516,635). Basically the Examiner asserts that "Ekins *et al.* discloses the placement of tagged microspheres onto a surface to form an array upon which multiple binding assays may be performed" (see p. 2 of the 9-7-99 Office Action).

Ekins is directed to compositions and methods for binding assays. In Ekins, a surface is spotted with immobilized "capture binding agents", comprising binding sites specific for a target analyte. The target analyte is added and "developing binding material" (such as an antibody) with a label (such as a fluorescent microsphere) is added. As described at col. 4, line 40 of Ekins *et al.* the microsphere is used "as the label for the developing binding material, or for the capture binding agent and the developing binding material". Furthermore, "[w]hen both the capture binding agent and the developing binding material are labelled with fluorescent microspheres, different dyes will of course be used in the two sets of microspheres" (col. 4, lines 57-60). Accordingly, only a single class of antibodies is bound to a particular microsphere. The purpose of the microsphere is to serve as the label.

As outlined above, Ekins fails to teach each and every element of the claims of the present application. Applicants respectfully remind the Examiner as stated by the Federal Circuit in In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990), that "[f]or a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference."

Claims 1, 7 and 14 of the present invention are directed to methods and compositions comprising a substrate with a surface comprising discrete sites and a population of microspheres comprising at least a first and a second subpopulation, each subpopulation comprising a bioactive agent and an identifier binding ligand that will bind a decoder binding ligand such that the identification of the bioactive agent can be elucidated.

Applicants submit that Ekin *et al.* fails to teach a microsphere that 1) comprises a bioactive agent and 2) an identifier binding ligand that will bind a decoder binding ligand. The

microspheres of Ekin *et al.* contain a single class of antibodies and a fluorescent label. The label on Ekins' microspheres is neither a bioactive agent nor an identifier binding ligand that will bind a decoder binding ligand; the only remaining component of Ekins' microspheres is an antibody. Thus, the microspheres disclosed in Ekins *et al* are distinct from the microspheres described in claims 1, 7 and 14 of the present application.

Claims 2, 6 and 13 are directed to methods and compositions comprising a substrate with a surface comprising discrete sites and a population of microspheres comprising at least a first and a second subpopulation, wherein each subpopulation comprises a bioactive agent and does not comprise an optical signature.

As described above, the microspheres of Ekins *et al.* are directly labeled. Thus, they contain an optical signature. As described in claims 2, 6 and 13, however, the microspheres do not comprise an optical signature. Accordingly, Ekins *et al.* fails to anticipate the invention of claims 2, 6 and 13.

Claim 8 is directed to a method of decoding a composition comprising providing an array composition comprising a substrate with a surface comprising discrete sites and a population of microspheres comprising at least a first and a second subpopulation, wherein each subpopulation comprises a bioactive agent, wherein the microspheres are randomly distributed on the surface and adding a plurality of decoding binding ligands to the array to identify the location of at least a plurality of the bioactive agents.

As described above, the microspheres of Ekin *et al.* contain a single class of antibodies and a fluorescent label. As such, there is no teaching of adding a decoder binding ligand or plurality of decoder binding ligands to the array to identify the location of the bioactive agents. Accordingly, Ekins fails to teach each and every element of claim 8.

In addition, the labeled microspheres of Ekins *et al* are attached to antibodies; the antibodies are directed to a particular antigen. As described above, the capture agent is immobilized on a substrate in microspots and when bound to its respective target, provides for binding to the developing binding material (antibody) bound to the microsphere. Thus, the

microsphere is distributed on the array in a very ordered fashion; it will only attach where the developing binding material has binding sites, namely the capture agent and/or target.

However, all of the present claims recite that the microspheres (that are themselves distinguishable from any teaching in Ekins *et al*) are randomly distributed on the surface of the substrate. Accordingly, Ekins fails to teach yet another element of the presently claimed invention.

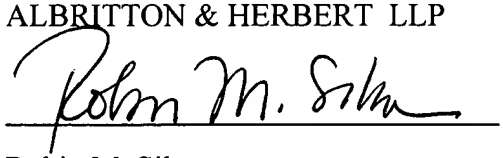
Accordingly, Applicants submit that Ekins *et al.* fails to teach each and every element of the presently claimed invention and as such is not an anticipatory reference. Applicants respectfully request the Examiner to withdraw the rejections under 35 USC §§ 102 (b) and (e).

CONCLUSION

Applicants submit that the claims as amended are in form for immediate allowance and the Examiner is respectfully requested to early notification to that effect. The Examiner is invited to contact the undersigned at (415) 781-1989 if any issues may be resolved in that manner.

Respectfully submitted,

FLEHR HOHBACH TEST
ALBRITTON & HERBERT LLP



Robin M. Silva
Reg. No. 38,304

Four Embarcadero Center
Suite 3400
San Francisco, CA 94111-4187
Telephone: (415) 781-1989
Dated: 7 February 2000
1006070

APPENDIX- CURRENTLY PENDING CLAIMS

1. (Amended) An array composition comprising:

a) a substrate with a surface comprising discrete sites; and

b) a population of microspheres comprising at least a first and a second subpopulation, wherein each subpopulation comprises:

i) a bioactive agent; and

ii) an identifier binding ligand that will bind a decoder binding ligand such that the identification of the bioactive agent can be elucidated;

wherein said microspheres are randomly distributed on said surface.

2. (Amended) An array composition comprising:

a) a substrate with a surface comprising discrete sites; and

b) a population of microspheres comprising at least a first and a second subpopulation, wherein each subpopulation comprises a bioactive agent and does not comprise an optical signature, wherein said microspheres are randomly distributed on said surface.

3. A composition according to claim 1 or 2 further comprising at least one decoder binding ligand.

4. A composition according to claim 1 or 2 wherein said bioactive agents are nucleic acids.

5. A composition according to claim 1 or 2 wherein said bioactive agents are proteins.

6. (Amended) A method of making a composition comprising:

a) forming a surface comprising individual sites on a substrate;

b) randomly distributing microspheres on said surface such that said individual sites

contain microspheres, wherein said microspheres comprise at least a first and a second subpopulation each comprising a bioactive agent and do not comprise an optical signature.

7. (Amended) A method of making a composition comprising:

a) forming a surface comprising individual sites on a substrate;

b) randomly distributing microspheres on said surface such that said individual sites contain microspheres, wherein said microspheres comprise at least a first and a second subpopulations each comprising:

i) a bioactive agent; and

ii) an identifier binding ligand that will bind a decoder binding ligand such that the identification of the bioactive agent can be elucidated.

8. (Amended) A method of decoding an array composition comprising:

a) providing an array composition comprising:

i) a substrate with a surface comprising discrete sites; and

ii) a population of microspheres comprising at least a first and a second subpopulation, wherein each subpopulation comprises a bioactive agent;

wherein said microspheres are randomly distributed on said surface;

b) adding a plurality of decoding binding ligands to said array composition to identify the location of at least a plurality of the bioactive agents.

9. A method according to claim 8 wherein at least one subpopulation of microspheres comprises an identifier binding ligand to which a decoding binding ligand can bind.

10. A method according to claim 8 wherein said decoding binding ligands bind to said bioactive agents.

11. A method according to claim 8 wherein said decoding binding ligands are labeled.

12. A method according to claim 8 wherein the location of each subpopulation is determined.

13. (Amended) A method of determining the presence of a target analyte in a sample comprising:

a) contacting said sample with a composition comprising:

i) a substrate with a surface comprising discrete sites; and

ii) a population of microspheres comprising at least a first and a second subpopulation each comprising a bioactive agent and do not comprise an optical signature;

wherein said microspheres are randomly distributed on said surface such that said discrete sites contain microspheres; and

b) determining the presence or absence of said target analyte.

14. (Amended) A method of determining the presence of a target analyte in a sample comprising:

a) contacting said sample with a composition comprising:

i) a substrate with a surface comprising discrete sites; and

ii) a population of microspheres comprising at least a first and a second subpopulation each comprising:

1) a bioactive agent; and

2) an identifier binding ligand that will bind a decoder binding ligand such that the identification of the bioactive agent can be elucidated;

wherein said microspheres are randomly distributed on said surface such that said discrete sites contain microspheres; and

b) determining the presence or absence of said target analyte.

Please add the following new claims:

- -15. The composition according to claim 1 or claim 2, wherein said discrete sites are wells.

16. The method according to claim 6, claim 7, claim 8, claim 13 or claim 14, wherein said discrete sites are wells.- -.